UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/042,460	03/16/98	MORIN	G 015389003110

HM22/1013

GREGORY P. EINHORN
TOWNSEND AND TOWNSEND AND CREW
TWO EMBARCADERO CENTER
8TH FLOOR
SAN FRANCISCO CA 94111

EXAMINER	
KAUSHAL, S	
ART UNIT	**PAPER NUMBER**
1633	16

DATE MAILED: 10/13/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/042,460	MORIN et al
Examiner	**Group Art Unit**
SUMESH KAUSHAL	1633

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-19* is/are pending in the application.

Of the above, claim(s) *5-9, 15, and 16* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4, 10-14, and 17-19* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7, 14*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Applicant's election of Group-I in Paper No. 15 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 5-9 and 15-16 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected groups. Claims 1-19 are pending. Claims 1-4, 10-14 and 17-19 are examined in this office action.

Priority

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 and 120 as follows: The instant application claims priority US and PCT applications which does not provide written description of SEQ ID: 1, 2 or mTERT. Furthermore, claiming priority to an inappropriate earlier filing date would leads a shorter patent term, which could be of disadvantage to applicants.

The second application (which is called a continuing application) must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the continuing application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-4, 10-14 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was **not described in the specification** in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession of the claimed invention**.

Claims 1-4, 12-14 and 17-19 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, **to make and/or use** the invention.

Claims are drawn to an isolated, purified or recombinant nucleic acid encoding mTERT protein having a molecular weigh of between 50-150 kDa and specifically bind to an antibody that bind to a protein comprising SEQ ID 2 or subsequence thereof. Claims are also drawn to an isolated nucleic acid wherein the calculated molecular weight of encoded mTERT protein is about 127 kDa, wherein mTERT protein having alt least 60% identity to SEQ ID 2 and encodes at least five contiguous amino acids of mTERT. Furthermore, claims are drawn to transfected cell comprising heterologous nucleic acid encoding mTERT protein or subsequence thereof, capable of specifically hybridizing to SEQ ID NO:1. Claims are further drawn to transgenic cell where endogenous mtRT

gene has been mutated by recombinant means with nucleic acid comprising at least a subsequence of a nucleic acid encoding mTRT gene, wherein the cell is deficient in at least one mTRT or telomerase activity and/or completely lacks all mTERT or telomerase activity. In addition claims are drawn to expression vector (as claimed) wherein the expression vector is pGRN227 and pGRN188.

Applicant is referred to the Interim guidelines on **Written Description** published June 15, 1998 in the Federal Register, Vol. 63, No. 114, pp. 32639-32645 (also available at www.uspto.gov). In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. Therefore, the inquiry required by this portion of the written description guidelines is interpreted to be whether all isolated purified or recombinant nucleic acid or subsequences thereof, encoding all mTERT proteins ranging from 50-150 kDa have been described. The inquiry also required whether the specification describes the transgenic cells and progeny thereof wherein the cell comprises an endogenous mTERT gene which has been mutated by recombinant means with nucleic acid comprising at least a subsequence of a nucleic acid encoding mTRT gene, wherein the cell is deficient in at least one mTRT or telomerase activity and/or completely lacks all mTERT or telomerase activity. The inquiry also required whether the specification describes the claimed pGRN227 and pGRN188 expression vectors. In this case, the few disclosed embodiments are not representative of enormous number of products claimed. The specification only disclosed nucleic acid SEQ ID 1 and amino acid SEQ ID 2 and fails to describe the any and all mTERT subsequences thereof, encoding a protein having calculated molecular weight of between 50-150 kDa or 127 kDa. The specification fails to describe any and all mutant transgenic cells wherein an exogenous mTRET gene is inserted. In addition, the specification also fails to clearly describe the claimed pGRN227 and pGRN188 vectors (page 98 line 29-31, page 99 line 1-17). The limited disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that applicants were in possession of the huge genera recited in the claims at the time the application was filed. It is not clear from the

specification that the applicant possessed any and all variants of mTERT nucleic acid, amino acid sequences, expression vector and transgenic cells because the specification does not disclosed or identify the claimed subject matter. Thus, it is concluded that the written description requirement is not satisfied for the claimed genera.

The specification fails to provide guidance to **make and use** any and all nucleic acid encoding mTERT proteins having molecular weight between 50-150 kDa or about 127 kDa, and having at least 60% identity to amino acid of SEQ ID 2. The specification also fails to provide guidance to make and use the transfected cells (as claimed) wherein the cell comprises an endogenous mTERT gene which have been mutated by recombinant means with a subsequence of mTERT gene and the transgenic cell is deficient in at least one mTERT or lacks all mTERT or telomerase enzyme activity. In addition the specification fails to provide guidance to make and use pGRN227 and pGRN188 expression vectors.

The specification teaches that the methods of making polypeptide are used for the purpose of producing polypeptide that can be used to make antibodies against the claimed polypeptide. As recited in claims 1 and 17 the amino acid sequence can differ from one encoding part of SEQ ID: 2 as much as 40%. If the differences are evenly distributed, mismatches in no-wobble bases, then almost every amino acid could be different, altering the sequence with insertion/deletion differences further complicates the matter.

One skilled in the art would be able to practice the invention for producing recombinant polypeptide subsequently used for making antibodies against peptides, that are part or all of a polypeptide encoded by DNA encompassed by claims, assuming that the amino acid sequence was known. However, the specification does not identify any polypeptide whose sequence is within the window encompassed by the claim other than that set forth in SEQ ID NO: 1. Furthermore, it is unclear which, if any, of the amino acid sequence variants of claimed polypeptide or peptide

fragments that could be encoded by the polynucleotides encompassed by the breadth of the claims could be used to make antibodies that recognize the claimed polypeptide. It is not clear that an antibody that recognizes a peptide sequence differing in almost every amino acid would bind to the claimed polypeptide or peptide fragment, and not preferentially recognize a peptide sequence derived from another unrelated polypeptide present in a sample. It is unclear how one skilled in the art could predict which of all the possible variant amino acid sequences are capable of binding to an antibody that binds to a protein comprising SEQ ID NO 2, and the specification provides no guidance on the matter.

It is known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Furthermore, one must engage in "case to case painstaking experimental study" to determine active variants (see page 7). Consequently, excessive trial and error experimentation would be required to identify the necessary nucleic acid sequence derivatives encoding a biologically active polypeptide with an amino acid sequence differing from SEQ ID NO: 2, since the amino acid sequence of such polypeptide could not be predicted *a priori*. Thus, in view of lack of specific guidance in the specification, the skilled artesian at the time of filing would be unable to use the claimed invention, without an excessive and undue amount of experimentation.

In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic

sequences may not find sufficient support under 35 USC 112, 1st para., if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. This is the case here, where specification discloses only a single amino acid sequence(s), SEQ ID NO: 2, for a polypeptide having the necessary properties for the disclosed uses, i.e. encoding an active mTERT protein or a polypeptide that possess telomerase activity, and provides no guidance on predicting polypeptide variants of SEQ ID NO: 2, which would be suitable for the disclosed use. Therefore, only polynucleotide, polypeptide, expression vector and host cells comprising nucleotide and amino acid sequences of SEQ ID 1, but not the full breadth of claimed invention is enabled.

Furthermore, the specification fails to provide guidance to make and use any and all transfected cells (as claimed). The specification articulates that transgenic cells can express an exogenous recombinant mTERT gene wherein one or several units of endogenous telomerase, telomerase RNA moiety and/or telomerase associated proteins have been first deleted or inhibited before the introduction of exogenous murine telomerase activity (page 111, line 28-31, App.Spec.). The mTERT gene can be "knocked out" using conventional techniques usually involving homologous recombination (page 112, line 4-12). However, it is not clear from the specification that the applicant possessed even a single transfected cell wherein any and all components of telomerase complex have been knocked out by recombinant means and an exogenous mTERT gene have been transfected. The specification fails to provide guidance to knock out any and all endogenous units of telomerase, telomerase RNA moiety and/or telomerase associated proteins, which results in lack of at least one and/or all mTERT or telomerrase activity in any cell. The state of the art at the time of filing was such that functional "telomerase complex" consists of telomerase protein, telomerase RNA moiety and telomerase associated proteins which are essential for the maintenance of telomere length (Lundblad, PNAS 95:8415-8416, 1998, page 8415, col.1 para.2, page 8416 col.1, para 2-3). The specification fails to provide guidance as to which components of telomerase complex are mutated

in transgenic cells in order to make the cell deficient in at least one or all mTERT or telomerase enzyme activity. Furthermore, the phenotype of targeted mutations by a homologous recombination have not always been as predicted from the knowledge of the nature of the gene product and its pattern of expression (Rossant et al , Phil. Trans. R. Soc Lond. B. 339:137-254, 1993; page 71 col.2 par.2). Thus, in view of lack of specific guidance in the specification, the skilled artisan at the time of filing would be unable to use the claimed invention, without an excessive and undue amount of experimentation.

In addition, as set forth in *In re Fisher,* 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and **distinctly claim the subject matter** which applicant regards as the invention.

The instant claims are indefinite because it is unclear what is encompassed by the claims since the specification does not define how "identity" is to be calculated and the art has not recognized one way of calculating homology. Homology (identity) is calculated for consecutive nucleotides but may or may not include gaps. Homology may be calculated relative to the query or matching sequence. These alternative means of calculating are important because they determine what, for example 95% means. Consider two sequences: ACTGTAC and ACAC. These can be compared in four ways. The example below illustrates how defining identity can influence the breadth encompassed by the claim. Query represent a single sequence being searched. Match represents a sequence found which matches the specific query.

Match:	**ACGTAC**	**4/6=67%**	**ACGTAC**	**2/6=33%**
	|| ||		||	
Query:	**AC--AC**	**4/4=100%**	**ACAC**	**2/4=50%**

Note that in present situation, homology, while used in the specification, like wise not defined.

The instant claims are indefinite because metes and bounds of nucleotide sequence and amino acid sequence (as claimed) are not clearly defined. The instant claims fails to recite the limitation which define the nucleic acid sequence of claimed SEQ ID NO(s) in its portion or its entirety. Providing subsequent nucleotide location of claimed nucleotide sequence(s) is remedial.

Claim 1, 2 and 4 are indefinite because claims recite " about" or "at least about". It is not clear what about or at least about comprises.

Claim 1, 10 and 17 are indefinite because claim recites "subsequence thereof". Claim 12 is indefinite because claim recites "progeny thereof". It is not clear what "thereof" refers to.

Claims 11 and 17 are indefinite because the specification fails to define "hybridizing under stringent conditions" as one set of conditions. The specification only generalized the stringent hybridization conditions for nucleotides less than or more that 50 nucleotides (page 91 line 11-30). However, the specification fails to define the specific stringent hybridization conditions requires for nucleic acid fragments of SEQ ID: 1 that has at least 60% sequence homology to amino acid sequence of SEQ ID NO 2.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 1, 2, 4, 10, 11 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Meyerson et al (Cell 90:785-795, 1997). Meyerson et al teaches amino acid subsequences and at least five contiguous amino acid sequences of SEQ ID NO:2. (see PTO sequence search report 8/16/99). In addition, the DNA described in prior art would hybridize to the nucleotide of SEQ ID NO:1 at some level of stringent conditions because the stringent condition has been described in instant application. Thus the cited art anticipated the claimed invention.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 1 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of SEQ ID NO: 2 of copending Application No. 09/128,354, 09/052,864, 09/052,919, 08/974,549, 08/911,312, 08/912,951, 08/854,050 (SEQ ID:225). Sequence search reveled that sequences enlisted in the above mentioned pending US patent application have 61% sequences identity to the amino acid sequences of SEQ ID NO:2 of instant application ('460). The above mentioned US applications are currently unavailable to determine all possible double patenting issues. The applicants are requested to supply a copy of claims of the above mentioned US applications to examine the double patenting issues. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM . If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brian Stanton Ph.D. can be reached on (703) 308-2801. The fax phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

Sumesh Kaushal

Art Group 1633

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER